GENERALIZED TELANGIECTASIA IN ASSOCIATION WITH SYPHILIS, WITH THE PATHOLOGICAL PICTURE OF PERIPHERAL VASCULAR SCLEROSIS.

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The case of generalized telangiectasia which forms the basis of the present study, occurred in the practice of Dr. John Tanner Holmes, formerly instructor in dermatology and syphilology in this department. It is through his courtesy in transferring the patient to the care of the University Hospital at the close of his connection with this clinic that the author is enabled to present the following report:

Generalized telangiectasia of the cutaneous bloodvessels is well recognized as one of the rarest of dermatological conditions. Joseph,[1] in *Mracek's Handbuch* (1904), mentions 9 reported cases. Subsequent studies, among which should be mentioned those of Mosny and Malloizel,[16] Ehrman,[17] [18] Lanceplaine,[15] Colcott Fox,[20] Trawinski,[21] Fearnsides,[22] Frick,[23] and others have, however, more than trebled this number. The case of angioma serpiginosum described by Wise[24] bears certain resemblances to the author's case, and will be discussed later. The recognition of the condition as a morbid entity is not as yet complete, and while many of the reports accord in essential particulars the etiology is as yet obscure. In the absence of satisfactory conceptions on this point, classifications of a descriptive or morphological type cannot escape an element of vagueness and uncertainty. In the hope of placing the case under discussion in as definite a relation as possible to those presented by other investigators, critical analysis of the literature is deferred until the findings in the present case are detailed.

The patient is a widow, aged thrity-four years, clerk by occupation, who came under observation complaining of spreading redness on the arms, legs, and body of five years' duration.

History. *Family History.* In direct and collateral lines of descent this is negative. Special inquiry into evidences of hereditary syphilis, hemophilia, familial tendency to epistaxis, vicarious menstruation, evidences of cardiovascular degeneration, such as apoplexy, cardiac weakness, etc., and nevus formation failed to reveal anything of interest.

Personal History. Patient was of normal birth. Good health as a child, with good recoveries from ordinary children's diseases. At nine years of age she began to suffer from nose-bleeding. The attacks averaged one a week and showed a certain periodicity. The hemorrhage was severe, the blood "gushing from the nose and spattering those about who tried to help." The patient states that it could only be controlled by putting her feet in hot water and tying cords tightly about her arms and legs. This recurrent epistaxis ceased abruptly with the patient's first menstruation at the age of twelve years, and she cannot recall a single attack since. Menstruation is normal in amount; flow three days; regular; no pain. A small telangiectatic nevus below the right eye has been present and undergone no change since she can remember.

Patient married at twenty-one years; has two living healthy children, both normal births; no miscarriages; no deaths. So far as she knows her husband was healthy up to final illness (aged thirty-two years at death).

Husband was examined as an out-patient in the neurological clinic of the University Hospital some time before his death, with the following history and findings (appended from the records through the courtesy of Professor Camp): *Complaint*, stomach trouble with pain and attacks of vomiting, frontal headache, memory defect, irritability, and fatigue. *Examination* showed unequal pupils, slow reaction to light, pupils dilate again; no choked disk; no sensory changes; deep reflexes normal. The husband was later operated upon, according to the patient's statement, at another hospital, a gastro-enterostomy being done, with fatal termination. No pathological change was said to have been discovered in the abdomen. No Wassermann reaction on either blood or spinal fluid was obtained in the University Hospital, but the presumptive diagnosis with the above findings is tabetic gastric crises.

The patient denies extramarital exposure, and has never, so far as she knows, presented evidences of active syphilis, although she was much troubled by "canker sores" five or six years ago. She has never been nervous and always of a matter-of-fact, placid, almost phlegmatic temperament. There is nothing in the history to suggest either hyper- or hypothyroidism, although special inquiry was made. No rheumatism, no urinary disturbances, no hemorrhoids or rectal bleeding. Three years ago (two years after onset of present trouble) she had an attack of mumps, which was said to have affected the ovaries, but made a good recovery. Never uses alcoholic liquors, has no dietary idiosyncrasies and no digestive disturbances. Nothing notable about occupation or habits except that she has been much on her feet. She is very constipated. Patient has never shown any special vasomotor instability, such as a tendency to blush.

Present Trouble. Began five years ago, three years before her husband's death. Dorsum of both feet first involved, two or three small pink spots becoming confluent, and a diffuse redness spreading up the leg. Wrists involved at about the same time, the condition spreading upward on both arms and legs, and involving the trunk last. At no time have there been any signs of the trouble upon the face or the palms of the hands. While the telangiectases were spreading the patient gained fifteen pounds in weight, and from a rather well-nourished woman has become somewhat obese. For the last four years the patient has suffered much from headaches and a sense of fulness, and from a "drawn feeling" in the head and eyes. Dizzy at times for the last four years, but for the last two has been much worse, and patient has noticed it while walking. Has had to use aspirin for the relief of the headache during the past year. Skin itches slightly, and there is some scaling. Troubled with chilly feelings, less marked at the present time. Vascular condition seems about stationary for the past few months. Patient complains that she cannot perspire. Hands and feet never swell, are always warm, and she is not short of breath on ordinary exertion. She has noticed that the redness is more marked when the parts are dependent, and that when she rises in the morning the affected skin is almost white.

General Physical Examination of Patient. A decidedly fleshy woman, well developed, in early middle life. Pupils somewhat sluggish to light, accommodation normal. No eye signs of exophthalmic goitre. Visual fields normal. Flush over the face. *Thorax* hyperresonant; breath sounds markedly accentuated in left upper portion. *Heart* markedly enlarged; impulse heaving; apex in fifth intercostal space, anterior axillary line. Tic-tac rhythm; no murmurs. *Abdomen* negative. *Pelvis:* some suffusion of mucosa of portio and vagina, otherwise negative. *Pulse* normal; radial artery negative.

Dermatological Examination. *Face* slightly suffused over the flush area; slight capillary dilatation. A pin-head papular nevus forms the centre of a small spider angioma below the outer canthus of the right eye. *Scalp,* marked seborrheic dermatitis; no telangiectases; no atrophy; hair fairly abundant. Port-wine nevus at the nape of the neck not conspicuous. *Skin,* except for a few pigmented nevi and the telangiectatic lesions to be described, presents no notable abnormality.

Special Lesions. The telangiectasia of which the patient complains is generalized over the larger part of the body, but with marked variations in the intensity of the involvement. The scalp, neck and shoulders and the palms of the hands and thicker portions of the soles seem to be the only entirely free areas. The backs of hands and the face and the flexor surfaces of the arms are relatively free. In the main the process is diffuse, but macular involvement of some of the comparatively normal skin is present, and deeper red patches are in places superposed upon areas of moderate telangiectasia, as, for example, over the buttocks. In general the configuration of the dilated venules is arborescent, stellate, or lace-like. The degree of dilatation varies greatly. On the legs below the knees, delicately beautiful telangiectatic figures of the arborescent type are visible with the naked eye. Elsewhere, naked-eye examination gives only impressions varying from that of an exaggerated *cutis marmorata* to the appearance of a reddish or livid mottling or an extensive blotching suggestive of hypostasis or suggillation, in which the telangiectasia is only visible with the aid of a lens. Four types of lesions are distinguished on close examination. The first is the diffuse or mottled, dark-red to purplish flush over extensive areas, such as the entire extensor surfaces of both arms from the shoulders to the wrists. All the larger sites presenting this type of involvement, including the buttocks and lower abdomen and the thighs above the knees, exhibit the arborescent configuration imperfectly, which leads to various degrees of mottling. Below the knees the telangiectasia takes the second form, approaching the type of the nevus araneus, with confluence of the individual capillary and stellate groups to form a continuous tracery. The third type of lesion is the macule, which is usually seen on comparatively free areas, but which is occasionally superimposed upon the diffuse lesion. The macules are oval or irregular in outline, do not exceed a centimeter in diameter, and show only a diffuse redness to the naked eye, without any suggestion of special structure. They are not elevated or depressed, have no sharp border, no involuting or atrophic centre. The fourth type of lesion is found only over the shoulders from the deltoid region to the middle of the upper arm, and consists of pin-point purplish or reddish angiomatous puncta which, under the lens, look like glomerular tufts or minute senile angiomata. They are scattered about irregularly over the surface mentioned and exhibit no definite configuration.

In addition to the foregoing types of vascular lesions there is a single, oval, annular patch of brownish hyperpigmentation, about 12 mm. in diameter, to the right of the median line and about 2 inches below the umbilicus. This shows neither induration nor atrophy. No other lesion of this type could be found on the remainder of the body. All the involved parts of the skin, but especially the extremities, showed a slight furfuraceous scale. In a single small patch below the outer condyle of the right humerus the scale was thicker and more adherent, and there was a suggestion of atrophy. This patch later disappeared and the skin resumed the appearance of the telangiectatic surroundings.

There were no suggestions of annular or gyrate configuration, of white spots, of central involution, of induration or nodule formation of edema, purpuric hemorrhage, atrophy, or follicular changes associated with the telangiectasia.

Inspection of the lesions, region by region, reveals the following additional points of interest. Even in apparently normal regions, close inspection discloses an involvement of the deeper vessels, and occasional tortuous venules and loops can be made out. The symmetry of the diffuse type of involvement is in marked contrast to the asymmetry of the macular type. Of the latter lesion, five patches occur below the left scapula and an equal number low on the right buttock. There are four typical macules on the left side of the abdomen and one over the inner condyle of the left humerus which are without fellows on the right side. The region of the mammary glands is almost the sole site of thoracic involvement anteriorly. The arborescence is radiating, with the nipple as a centre, and there is marked accentuation in and immediately around the areola. Another striking feature is the marked accentuation of the process in scars. The vaccination scar is the site of a vivid telangiectasia, and the striæ albicantes are made conspicuous in the same way. Two symmetrical patches of lichenification and hyperpigmentation on the adjoining surfaces of the thighs, due to chafing, are free from involvement, the ectasia being sharply limited at their borders. Along the anterior and outer surfaces of the thighs are typical deep, spider-web varicosities of the larger superficial veins forming a radiating, dusky purple network beneath the red mottling and tracery of the minute capillaries. This is presumably simply a phase of a general accentuation of the process in the more dependent portions of the body, which is easily apparent. The deep veins of the legs, however, show no external signs of involvement.

Mucous Membranes. Negative to ordinary inspection.

Glandular System. Left epitrochlear palpable; one large gland in left inguinal group. Otherwise negative.

Osseous System. No nodes on long bones, no tenderness, no bone changes suggestive of lues hereditaria.

Special Reactions on the Part of the Skin Lesions. Pressure. In practically all parts of the body, sufficiently heavy pressure caused a momentary disappearance of the erythema. The length of time that the area pressed upon remained blanched was greatest where the ectasia was moderate. Under glass pressure the red area first became yellow and then pale. In the most intensely affected parts all the pressure that could be brought to bear, scarcely sufficed to blanch the skin completely. Rapid stroking in even markedly involved regions, such as the arms, was fully as effective. *Posture* had a very marked effect. The backs of the hands, ordinarily little affected, showed marked arborescent reddening when the arm hung at the side for some time, and the hand and forearm well above the wrist could be blanched by elevation above the head. The legs paled distinctly on elevation. *Interference with venous return* accentuated the dilatation. *Cold* in the form of the ice-bag caused slight blanching, persisting after the removal of the bag itself for quite an appreciable interval, after which erythema seemed to develop, so to speak, between the original arborescences, forming a distinctly brighter flush. *Heat* was followed almost at once by an excessive reaction in the form of blotchy erythema, as compared with a normal arm used as control. *Temperature to touch:* As a rule the skin was warm but not excessively so. The extremities were seldom cold even in a cold room, and not distinctly cyanotic. There was none of the blueness of vasomotor asthenia. *Hemorrhage:* As ascertained in the biopsies, it was no more profuse than from a normal skin, even without the use of adrenalin in the anesthetic. *Emotion* was entirely without effect.

CLINICAL LABORATORY FINDINGS. *Urine.* Three examinations, including a morning and evening specimen and one after diuresis (copious water), were negative for albumin, glucose, acetone, indican, bile, casts, blood, pus, crystalline sediment, and specific gravity.

Blood. Two counts, taken a week apart, gave the following results: (1) Reds, 5,580,000; whites, 7500; hemoglobin (Miescher), 88 per cent; (2) reds, 5,440,000; whites, 7250; hemoglobin (Meischer), 87 per cent.

Differential count: polymorphonuclears, 61 per cent.; small lymphocytes, 27 per cent.; large lymphocytes, 8 per cent; transitionals, 2 per cent.; eosinophiles, 2 per cent.; mast cells, none seen in 200 cells.

Coagulation Time. Two careful observations were made, two weeks apart, the first result being four minutes forty-five seconds, and the second four minutes; both results thus well within normal limits.

Blood-pressure. Four observations were taken, one week apart, using the Mercer and Faught mercury column instruments. Systolic pressure varied between the limits of 113 mm. and 128 mm.; diastolic between 90 mm. and 118 mm.

Wassermann Reaction. This could only be taken on the blood, the patient refusing a lumbar puncture. The reaction was positive once and negative once.

Urea Content of the Blood. This was determined through the courtesy of the medical service, and was found to be 0.32 gm. per liter. From the standpoint of nitrogen elimination, then, the renal function is apparently normal.

Stool examination was entirely negative.

SPECIAL INVESTIGATIONS. Believing that the value of this case as an etiological study of an obscure dermatosis would be greatly enhanced by expert judgment on certain special phases, the generous coöperation of the chiefs of the ophthalmological, otological, medical, neurological, and roentgenological departments of the University Hospital was enlisted in the preparation of the special reports which follow.

The examinations were planned to throw light on the following features of the case: (1) The condition of the cardiovascular system as a whole. (2) The condition of the nervous system with reference to any known organic or functional lesion that might bear on a possible vasomotor origin for the dermatosis. (3) The question of the existence of syphilis in this patient and its role, if any, in the picture of cutaneous vascular pathology which she presents. Incidentally the otolaryngological examination cleared up the question as to telangiectases on the mucous membranes of the upper respiratory tract, a point of special interest in view of the history of epistaxis in childhood and the known association of this condition with Osler's syndrome.

Otolaryngological Examination. This examination was performed by Professor R. Bishop Canfield, whose report is appended:

"The examination of the mucous membrane of the nose and throat reveals nothing abnormal, although when my attention was called to her condition by Dr. Stokes, I was inclined to think that I could detect a general suffusion of the mucous membrane of the nose. This was not marked enough, however, to consider abnormal. The ears show a marked decrease in bone conduction, although the high limits are normal. The fact that she retains good hearing in both ears makes this decrease in bone conduction typically luetic."

The examination of the fundus of the eye was performed by Professor Walter R. Parker, who in addition to finding the fields normal reports the following:

"*Ophthalmoscopic Examination.* O. D.; media clear. The head of the nerve is markedly congested, edges obscured; small central physiological cup; the lamina cribrosa are not seen. The head of the disk is elevated one to two diopters, but is not edematous. The veins are slightly engorged and tortuous; some arteriovenous compression; marked tortuosity of the smaller arteries. The retina is slightly edematous with marked striations, most marked in the vicinity of the disk; details of retina blurred. The foveal reflex is present. No marked choroidal changes.

"O. S.: the media are clear. The head of the nerve is markedly congested, edges obscured except down and out, all of which area is blurred. The head of the nerve is elevated from one to two diopters. Marked arteriovenous compression; distal dilatation. The veins are engorged and tortuous. The foveal reflex is present.

"Diagnosis. O. U.: active neuroretinitis with advanced arteriosclerotic changes."

The Neurological Examination. This proved still further the results of the two preceding examinations relative to the existence of syphilitic involvement of the central nervous system. Professor Carl D. Camp's report is as follows:

"Examined October 25, 1914. Sluggish pupillary reaction to light; absent knee-jerks and sensory changes strongly suggest the diagnosis of incomplete tabes dorsalis. The telangiectatic areas do not appear to have a metameric distribution, nor have they any definite relation to the distribution of peripheral nerves."

More specifically enumerated, the sensory changes included loss of Achilles tenderness and marked increase in the distances at which the patient could distinguish compass points. Graves' sign and conjunctival anesthesia were present. There was no loss of sensibility to touch, pin-point or pin-head, and she differentiated heat and cold promptly over the entire body.

In order to investigate the dilatation of the heart, which had been foreshadowed by physical examination, and the condition of the aorta, and to determine whether any mediastinal tumor existed, whose pressure upon the sympathetic ganglionic chain might be a factor in the production of a vasomotor palsy, Professor J. G. Van Zuwaluwenburg fluoroscoped the thorax and prepared an orthodiagraph. His report follows:

"*Fluoroscopic.* The heart is evidently enlarged, particularly the left ventricle, reaching to the left thoracic wall.

" *Dimensions:* Mr, 25; ml, 97; long, more than 142; transverse 91; area, undetermined.

"The shadow of the arch of the aorta is exceedingly dense, more so than should be expected. This is particularly notable along the right margin, about two inches above the right auricle. It is probably due to calcification of the aorta."

The findings of the physical and fluoroscopic examinations were confirmed as regards the heart by an electrocardiographic tracing taken by Dr. F. N. Wilson through the courtesy of Professor Hewlett. No other special finding was noted.

With a view to ascertaining whether a record of the flow of blood through the arm, as determined by the plethysmograph, would contribute anything of interest to an understanding of the dynamics of the patient's circulation, Professor A. W. Hewlett undertook such a study. His conclusions are quoted as follows:

"The records from the arm show a rate of blood-flow in the arm of between 2 c.c. and 2.5 c.c. per 100 c.c. arm volume; the primary pulse wave puts in about 0.5 c.c. of blood. Both of these are about the lower limits of normal. Tracings are characterized also by a rather unusual degree of reflection of the primary pulse wave.

"It is hardly possible with our present knowledge to interpret these findings satisfactorily, but they might be due to a rather marked constriction of the arterioles in the arm, without a corresponding change in the larger arteries."

Professor Hewlett's opinion, based on functional investigation, is a remarkable confirmation of the clinical findings as above enumerated and of the direct pathological study of the lesion itself as detailed below.

EXAMINATION OF THE PATIENT'S CHILDREN. The patient's children, both girls, aged ten and twelve years, were examined for stigmata of inherited syphilis and for signs of vascular ectasia. Neither showed essential stigmata of the former disease. The older girl presented very definite saber tibiæ with other suggestions of abnormal ossification, such as ulnar deviation of the middle fingers, some saddling of the bridge of the nose, and a high, narrow palatine arch. There were no telangiectases. The younger girl had a prominent forehead with a suggestion of bosses, marked ulnar deviation of the middle fingers, very striking scaphoid scapulæ, and some epiphyseal enlargement, especially of the distal ends of the femora. Both had a negative Wassermann. The findings could not be rated as more than suggestive; certainly not diagnostic. The bone conduction test for specific auditory nerve involvement, conducted by Professor Canfield, showed a marked decrease in bone conduction, with practically normal hearing in both children.

It is of interest to note that the younger girl presented a telangiectatic lesion of the nevus araneus type, about 1 cm. square, over the left scapula, about which no history could be obtained.

HISTOPATHOLOGICAL STUDY. With the consent of the patient a biopsy was performed, two pieces of affected skin being excised. The first consisted of a typical macular lesion below the left scapula. The second was taken from a region of typical diffuse arborescent telangiectasia about three inches below the right knee on the internal surface. The macular lesion was fixed in absolute alcohol and later transferred to 5 per cent. formalin. The piece from the diffuse area was fixed in 5 per cent. formalin alone. The material was embedded in paraffin and the sections cut at 10 microns. The stains employed were Unna's polychrome methylene-blue, polychrome-eosin, polychrome-acid orcein, polychrome-neutral orcein, Van Gieson, carbolmethyl-green pyronin (Unna-Pappenheim), and hematoxylineosin. The only essential difference observable between the two pieces of material was a more marked dilatation of certain of the vessels in the specimen from below the knee. The pathological changes were as follows:

Epidermis. On the whole the changes are not marked. Slight atrophic thinning was apparent with moderate hyperkeratosis. Occasional intracellular edema was noted, affecting especially the basal layer and the deeper portions of the rete Malpighii. Occasional polymorphonuclear and round cells had invaded the epidermis, the latter being the more numerous.

Corium. The vascular supply of the corium and hypoderm was the seat of the significant pathological changes. The capillary loops in the papillæ were markedly dilated, much as is seen in a psoriasis. The subpapillary vessels presented a variety of changes representing phases of the essential process of obliterative endarteritis and periarteritis of certain vessels with compensatory dilatation of others. In conjunction with these changes, varying degress of of perivascular round-cell infiltration have occurred. Topically enumerated, examples of the following changes were easily found in all the sections examined:

Simple endothelial swelling in normal or dilated capillaries;

endothelial proliferation, all degrees to total obliterative endarteritis; perivascular thickening, affecting media and adventitia of the larger arterioles, with normal endothelium; periarteritis with obliterative endarteritis; simple ectasia (compensatory?) in otherwise normal vessels; ectasia with endothelial swelling and various degrees of proliferation; ectasia with normal endothelium and perivascular thickening.

New formation of capillaries was well marked, and there were numerous examples of the formation of capillary tufts from the lengthening and doubling of single vessels upon themselves. These tufts lay with their long axes in the lines of least resistance in the connective tissue. The cellular infiltrate appeared with the earliest signs of endothelial swelling, and was associated in varying degree with all stages of the endarteritis and periarteritis. The infiltrating cells were uniformly mononuclear lymphocytes, often arranged in arcs and concentric rings around the affected vessels. In no case was the infiltrate massive in character. There were no hemorrhages, no pigment deposits, no perivascular edema, or other evidence of acute injury to the vessel walls. Typical fibroblastic proliferation was evident around some of the small vessels, but nothing in the least suggestive of a neoplastic change could be discovered. There was a marked general increase in mast cells throughout the corium, especially conspicuous in the deeper layers and about the larger capillaries. The collagen and elastin were not noticeably involved.

Hypoderm. A marked sclerosis of the larger arterioles was apparent, affecting the media and adventitia rather than the intima. Many of the vessels had walls at least as thick as their lumina. In them the endothelial involvement was evidently less intense, concentric rings of large pale-staining nuclei in the outer coats showing the process to be essentially periarteritic.

The series of figures presented with this study are drawn from actual fields, and depict stages in the endarteritis and periarteritis associated with various degrees of round-cell infiltration. In Fig. 1, endothelial swelling, the earliest stage of the process is practically the only change. Fig. 2 shows a perivascular round-cell infiltration well established, endothelial swelling in the dilated capillary which is cut in cross-section, and swelling of some of the endothelial cells in one of the capillaries cut in longitudinal section, with lack of involvement in the main stem. One of the branches of the main trunk forms a capillary tuft just beyond the limits of the field. Fig. 3 illustrates the beginning encroachment of the proliferating endothelium upon the lumen and the decided increase in connective tissue about even very small vessels. In Fig. 4 the endarteritis is well advanced, the perivascular infiltrate less conspicuous. Fig. 5 is typical of the stage of practically complete obliteration. Longitudinal and cross-sections of vessels were found, which would not have been out of place in a syphilitic primary lesion. Fig. 6 is

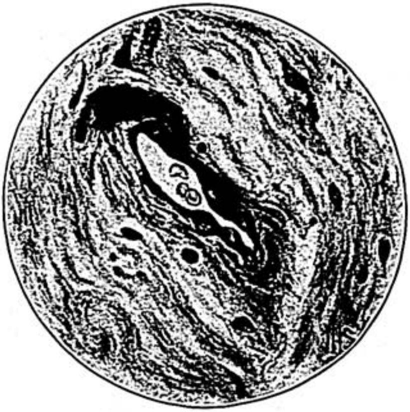

FIG. 1.—Capillary of the sub-papillary rete, showing endothelial swelling and a few perivascular round cells. Mast cells at the margin of the field. Polychrome methylene blue (Unna), Leitz $\frac{1}{12}$ oil-immersion objective.

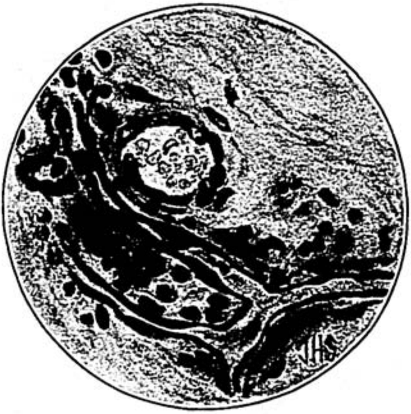

FIG. 2.—Capillaries, showing endothelial swelling and well-marked round-cell infiltration. Polychrome methylene blue (Unna), Leitz $\frac{1}{12}$ oil-immersion objective.

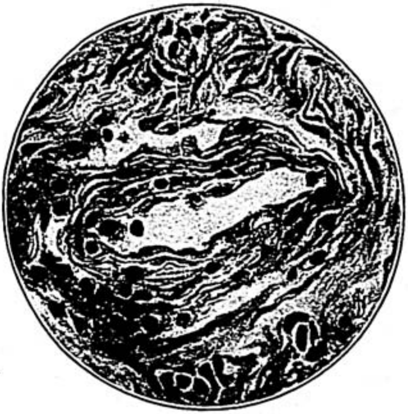

FIG. 3.—Perivascular fibrosis, endothelial proliferation, in a small vessel of the sub-papillary rete. Round cell collection to the left. Orcein-polychrome methylene blue (Unna), Leitz $\frac{1}{12}$ oil-immersion objective.

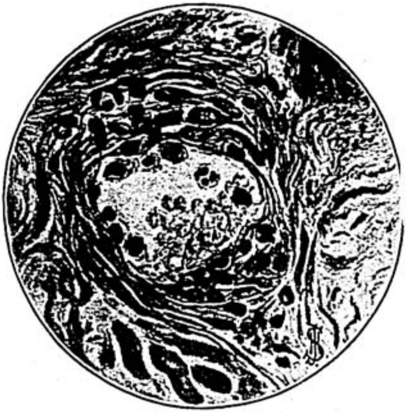

FIG. 4.—Endarteritis, partial obliteration. Infiltrate less marked. Orcein-polychrome methylene blue (Unna), Leitz $\frac{1}{12}$ oil-immersion objective.

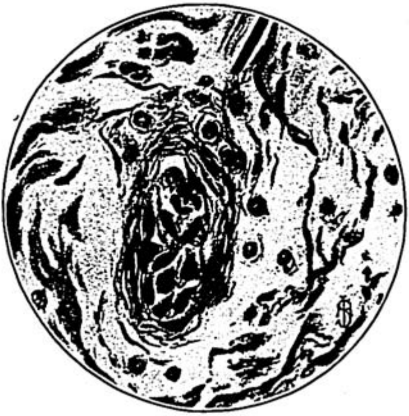

Fig. 5.—Endarteritis; practically total obliteration. Capillary fibrosis. A few scattered round cells. Orcein-polychrome methylene blue (Unna), Leitz $\frac{1}{12}$ oil-immersion objective.

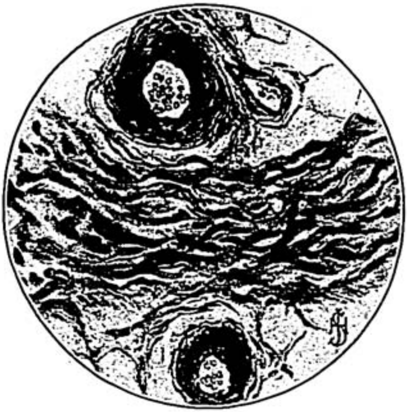

Fig. 6.—Sclerotic changes in the vessels of the hypoderm, confined to the media and adventitia, endothelium practically normal.

drawn from the subcutaneous fat of the specimen from the leg. The same condition was present in the excised macule.

SUMMARY OF THE CASE. The salient points in the foregoing presentation of my case of generalized telangiectasia may be summarized as follows:

1. A history devoid of hereditary or congenital elements bearing on present trouble.

2. Prior to marriage nothing of interest except epistaxis in childhood, ending with the establishment of menstruation.

3. Syphilis of the nervous system in the patient's husband (gastric crises).

4. The appearance in the wife eight years after marriage of seemingly idiopathic telangiectatic lesions in the skin, generalizing slowly through a period of five years. Lesions macular, punctate, and diffuse, the two latter symmetrical, the former asymmetrical in distribution. No other distinctive configuration, no symptoms, no notable secondary changes in the skin, such as hemorrhage, pigmentation, or atrophy. No involvement of mucous membranes.

5. The absence on examination of any demonstrable abnormality in the blood.

6. The absence on examination of any abnormality in the renal excretory mechanism.

7. The absence of any directly toxic influence known to have a degenerative effect on the cardiovascular system, such as alcohol, jaundice, lead.

8. The absence of evidence of vasomotor asthenia, of involvement of the nervous system other than that associated with tabes dorsalis or of involvement of the sympathetic system. Nothing to connect the distribution of the vascular phenomena with that of peripheral nerves.

9. The absence of any demonstrable abnormality of internal secretion—hyper- or hypothyroidism, pituitarism, ovarian or adrenal changes.

10. The presence of active syphilis in the patient in the form of involvement of central nervous system: active neuroretinitis; eighth nerve involvement; incomplete tabes dorsalis; positive, later negative Wassermann reaction on the blood.

11. Pathological changes in the cardiovascular system in the form of (*a*) hypertrophy of the heart and possibly a patch of calcification at the base of the aorta (electrocardiographic and fluoroscopic examinations), and (*b*) in the retina, demonstrable peripheral arteriosclerosis far in advance of the patient's years.

12. Experimental data (plethysmograph) tending to show a constriction of the peripheral arterioles in one of the most affected portions of the body (arm) without involvement of the deeper vessels.

13. Further evidence for a lack of extensive involvement of the deeper vascular trunks in the form of a normal blood-pressure.

14. Final microscopic demonstration in macular and diffuse types of skin lesions, of extensive endarteritis obliterans, and of periarteritis in the vascular supply of the skin, of the type often associated with syphilis. Accompanying this is a low-grade perivascular round-cell infiltration, new formation of vessels in the affected skin, and some ectasia (compensatory?) of vessels as yet uninvolved.

It is proper to remark that in thus seeming to summarize the case in favor of syphilis as the etiological factor, the writer is none the less aware of the virtues of conservatism, and of the possibility that something has slipped through the meshes of the net. In preference, however, to the blank confession of ignorance involved in the terms "idiopathic" and "essential," it would seem allowable to advance the most tenable hypothesis. In making syphilis the prime etiological factor in this case, due allowance should be had for a possible predisposition on the part of this patient's cardiovascular system to the injurious effects of a syphilitic infection. Of such vascular weakness or abnormality the epistaxis in childhood may have been an evidence. So far as this investigation shows, the telangiectatic lesions are scarcely to be interpreted as cutaneous syphilides in the strict sense. Rather the changes detailed above so strongly suggest those usually associated with syphilitic involvement of the cardiovascular system that the writer is inclined to look upon the case under discussion as one of peripheral vascular sclerosis in which syphilis has been the cardinal etiological factor.

DISCUSSION OF THE LITERATURE. The subject of generalized cutaneous telangiectasia is, as previously intimated, far from satisfactory elucidation. From the confused mass of reported observation and description, attempts have been made to select and distinguish certain groups, primarily upon the basis of certain clinical resemblances and associations. It would seem advisable for the present to rate these as syndromes rather than as clinical or pathological entities.

Among the notable contributions to the effort to group these clinical phenomena, Osler's[25] syndrome of hereditary recurrent epistaxis associated with cutaneous and mucous membrane telangiectases is one of the best known.* With this are included for the purposes of this paper the cases of multiple papular telangiectases on the skin and mucous membranes which have engaged the attention of British writers, notably F. P. Weber,[28] Kelly,[29] and others. Purpura annularis telangiectodes Majocchi constitutes another clinically well-defined group. Angioma serpiginosum of Hutchinson seems also to present a well-recognized clinical identity. Dubreuilh[30] and others have directed attention to the so-called senile angiomata. In spite of these attempts at classification there remains a residual group of cases which Lanceplaine[15] acting under Brocq's direction, undertook to systemmatize under the caption of essential or primary telangiectases, recognizing in the designation the existing ignorance of their etiology. A better illustration of the overlapping of the types enumerated could scarcely be desired than that afforded by Lanceplaine's inclusion of Majocchi's original cases in his discussion. Again, from the clinical description at least, Lanceplaine's thirteenth case might pass for one of angioma serpiginosum. Similar disagreements among authors can be noted in almost every paper on the dermatoses in question.

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* A case of acquired telangiectases reported by Osler[27] was accidentally overlooked by the writer until after the preparation of the statistical study. Patient was a male, very neurotic, exhibiting factitial urticaria, and having several attacks of possibly renal colic with hematuria while under observation. Telangiectases of wide distribution. Hands suggest Raynaud's disease. Spleen enlarged. Cardiovascular system not entirely normal apparently, but no definite diagnosis on this point or explanation of the cutaneous condition is offered. Vidal's and Levi's cases are cited.

With Ehrmann's[17 18] publication in 1907 of a report on four cases an effort to introduce an etiologically unified group of generalized telangiectasias with syphilis as a basis, was made. Trawinski,[21] in 1910, followed Ehrmann's lead in reporting another case of generalized telangiectasia associated with syphilis. In 1908 Colcott Fox,[20] in reporting a peculiar case of obscure etiology, attempted a general survey of the entire field, without, however, mentioning Ehrmann's work. Fox's division of the subject included (1) nevi, under which he grouped angioma serpiginosum, and (2) Majocchi's disease. He then adopted Lanceplaine's three groups: (1) telangiectases complicating various dermatoses, (2) telangiectases symptomatic of disturbances of the general circulation, and (3) essential or primary telangiectases. Lanceplaine's subclassification of the essential forms is based solely upon morphology, a weakness to which Fox calls attention. Fox himself included the senile angiomata of Dubreuilh among the essential forms. His fourth group is limited practically to Osler's syndrome. The etiological study of telangiectasia received a renewed impulse with the publication of a series of 6 cases by Fearnsides,[22] in 1912. In this series, chronic diarrhea with marasmus and edema form the background for the cutaneous manifestations. The most recent consideration of any of the above-mentioned groups is that of Wise,[24] which is based upon a clinical case of angioma serpiginosum, and contains a comprehensive review of the literature connected with that dermatosis.

In the effort to place my case in proper relation to those discussed by the authors mentioned above, I was impressed by the tentative character of most of the generalizations, and their application rather to the specific case than to any group as a whole. The absolute necessity for narrowing the field, led me to eliminate for the time being, for purposes of discussion, the well-defined groups, such as Osler's syndrome, Majocchi's disease, and angioma serpiginosum. An effort was made to collect, for comparison, the cases dealt with in the literature as belonging to the primary or essential group of acquired generalized telangiectasia. To this group, on the whole, rather than to any of the others mentioned above, except that of Ehrmann, my case seemed to bear the most resemblance. In place of the conventional abstract of the literature it was thought worth while to make a critical analysis of a combination of these nondescript or isolated cases and of the less well-known groups, such as those of Ehrmann and Fearnsides, in order to see whether a composite picture might not be forthcoming. In this composite picture it was hoped that etiological generalizations might stand out with enough distinctness to justify at least a partial discarding of the terms "essential" or "idiopathic." The usual difficulties which beset such a study from case reports were encountered in full measure, and were in themselves no small explanation of the reason why the etiology is still shrouded under the mystic term "essential." Several of the standard references in the literature, cited by one author after another, were hardly more than clinical notes or skeleton presentations. In spite of this difficulty, however, 33 cases, including the present one, were submitted to a parallel column analysis. The cases reported by the following writers constitute the material for this portion of the study: Tanturri[2] (1879) (Jullien's abstract); Vidal[3] (1880); Mandelbaum[4] (1882); Gastou[5] (1894); Morrow[6] (1894); Terrell[7] (1896); Levi et Le Noble[8] (1896); Chauffard[9] (1896); Kopp[10] (1897); Letienne et Arnal[11] (1897); Brocq[12] (1897); Levi et Delherm[13] (1901); Gaucher et Crouzon[14] (1902); Lanceplaine[15] (1904), three original cases (II, III, XIII); Mosny et Malloizel[16] (1905); Ehrmann[17] (1907), four cases; Hyde[19] (1908), case IV; T. C. Fox[20] (1908); Trawinski[21] (1910), Fearnsides[22] (1912), six cases; Frick[23] (1912), author's case (1914). Gastou, it should be recalled, reported two cases in the same discussion, a father and daughter. Details about the latter case were, however, very meager.

The findings are presented in groups, representing parts of a detailed topical outline into which each case was fitted. The outline proved to be too complete for a number of the less carefully worked-up cases, and accordingly only a few of the items carry figures covering the whole series of 33 cases. The totals represent the number of cases in which data are given.

FAMILY HISTORY OF PATIENTS. This was limited to the direct line of descent, and for practical purposes included only the parents.

Item.	Positive.	Negative.	Doubtful.	Total.
History of hereditary transmission .	1	21	0	22
Neuropathic heredity	1	12	0	13
Cardiovascular disease in parents . .	5	10	0	15
Syphilis in the parents	1	12	0	13
Other constitutional diseases in the parents (diabetes, 1; tuberculosis, 1, rheumatism, 1)	3	13	0	16

The single case of hereditary transmission and that of syphilis in the parents are one and the same, the combination occurring in Gastou's[5] two cases. The father developed telangiectases in association with cardiovascular and late central nervous manifestations. The daughter, whose mother sustained a typical series of syphilitic pregnancies, developed a localized telangiectasia in early life, which generalized rapidly after a pregnancy. The figures as a whole, however, negate the idea that there is any hereditary influence directly concerned in the transmission of telangiectases of the essential type from parent to child. On the other hand the indirect influence of a weakened cardiovascular resistance may be inferred to some extent from the fact that of 15 cases, one-third had a parentage in which one or both members developed serious involvement of the circulatory system in the course of their lives. The influence of other constitutional diseases can hardly be judged from these figures:

AGE INCIDENCE OF TELANGIECTASES.

Under 10 years	2 plus 4 (Fearnsides' syndrome).
10 to 20 years	3 “ 2 “ “
20 to 30 years	8
30 to 40 years	2
40 to 50	4
50 to 60 years	1
60 to 70 years	1

It would appear that the highest age incidence is in early adult life between the ages of twenty and thirty years. Fearnsides' syndrome was mentioned separately in these figures, because as a picture associated thus far mainly with a disease of children it seemed a little out of keeping in this detail with the problem presented by acquired telangiectasia in later life.

SEX INCIDENCE. Many writers have noted the preponderance of females over males in connection with the development of generalized telangiectasia. The results in this series show 22 females affected as against 11 males.

SYSTEMIC DISEASE IN THE PATIENT. This is taken to mean chronic systemic disease of a serious character. The acute exanthemata are, of course, excluded.

Syphilis	11
Chronic lead poisoning	1
Hyperthyroidism	2
Nephritis	3
Hemophilia	1
Arthritis	1
Diarrhea with edema (Fearnsides)	6
	25
Counted twice	3
Total	22

Of the 11 syphilitic cases, Gastou II[5] is not spoken of as syphilitic by the author, but the description of the case justifies the diagnosis of hereditary syphilis. Ehrmann IV[17] is not specifically diagnosed as syphilitic, but endarteritis and general arteriosclerosis, especially cerebral, were demonstrated at autopsy, and the case is included with three of undoubted specific infection. Lanceplaine III[15] presented Argyl-Robertson pupils, primary optic atrophy, and other symptoms of tabes, although not definitely denominated such in the report. Lanceplaine XIII is not rated in this table, although the patient had a history of Bartholinitis and an undiagnosed ulcer in the mouth.

Two points stand out conspicuously from this table. The first is the prominence of systemic diseases which have a well-known tendency to attack the cardiovascular system, in association with so-called "essential" telangiectases. Syphilis, plumbism, hyperthyroidism, or nephritis are present in 22 and possibly 23 out of 33 cases. Chauffard's[9] case of hemophilia was associated with purpura and other evidences of actual injury to the vascular system. While the exact mechanism by which a prolonged diarrhea with loss of fluid, in Fearnsides syndrome, affects the vessel walls, may be a matter for discussion, the definite association of stasis manifestations and exudation of fluid (edema) with the picture in his cases, seems to support the view that we have to deal with a direct insult to the vessels which manifests itself in part in the development of telangiectases. Without yielding too much to the attractions of the argument *post hoc propter hoc*, it would seem a legitimate conclusion that diseases of a known cardiovascular degenerative type may be in definite etiological relation to a cutaneous vascular disturbance heretofore regarded as idiopathic and "essential." The second point is subsidiary to this, and calls attention to the leading role played by syphilis as a cardiovascular degenerative influence and possible etiological factor in the production of many generalized telangiectasias.

ACTUAL CARDIOVASCULAR CHANGES DEMONSTRABLE BY EXAMINATION OR AUTOPSY. This is in effect an objective confirmation and amplification of the general data embodied in the previous table, and dealing with the cardiovascular system at large. Cardiovascular changes demonstrable: positive, 13; negative, 8; doubtful, 7; total, 28.

The cases grouped under the heading "doubtful" include four of Fearnsides' in which the patient presented no demonstrable lesion other than edema and stasis manifestations and did not come to autopsy. Vidal's[3] case presented merely "palpitation," Fox's[20] case had a bradycardia with vasomotor asthenia, and Tanturri's[2] case is reported to have had a weak pulse and stasis signs. As the table stands, nearly 50 per cent. had involvement of the cardiovascular system concomitant with the local lesion in the skin.

RENAL INVOLVEMENT. This was positive in only 3 cases, negative in 21, and doubtful in 1. This relatively rare association of renal insufficiency with cutaneous telangiectases would seem to relegate it to a subsidiary rank among etiological factors. It is impossible to determine definitely from the descriptions whether the renal disturbance was primary or was secondary to cardiovascular changes.

VISCERAL CHANGES.

Pulmonary (emphysema, pleural adhesion)	5 cases in 13
Hepatic	3 cases in 16
Gastro-intestinal	9 cases in 16
Spleen	1 case.

The gastric manifestations were largely symptomatic, such as hyperacidity in nervous patients and gastritis in alcoholics. *Apropos*, pulmonary symptoms, in Brocq's[12] case the telangiectases extended rapidly after a severe pneumonia, possibly as a result of cardiac strain incident to this particular infection.

DISORDERS OF THE CENTRAL NERVOUS SYSTEM. In view of the prominent part which supposed neurological factors have played in the opinions of various writers who have discussed etiological possibilities in generalized telangiectasia, the findings under this heading were of more than ordinary interest. A rough classification into functional and organic conditions was made. Where a definite neurological entity existed it was classed as positive. Where the patient was described as merely "nervous," the case was rated as doubtful.

FUNCTIONAL DISORDERS.

	Positive.	Doubtful.
Hysteria	3	3
Miscellaneous	3	3
Total	6	3

ORGANIC DISORDERS.

Syphilis of the nervous system	3
Alcoholic polyneuritis	1
Chronic lead poisoning	1
Convulsions and imbecility	1
No definite syndrome	1
Total	7

Of the functional cases, one occurred in a syphilitic. Of the organic cases it will be noted that 5 out of 7 were due to agents whose influence was also apparent in the form of cardiovascular changes. In other words, in these 5 cases the telangiectasia could scarcely be the result of central nervous disturbance. Rather the central nervous disturbance and the cardiovascular phenomena were effects springing from a common cause—syphilis, alcohol, lead.

DISORDERS OF INTERNAL SECRETION.

Hyperthyroidism	2 cases.
Climacteric	1 case.
Puberty	1 case (doubtful).
Ovariotomy	1 case.

The objection to the *post hoc* type of reasoning applies with full force to the last three cases given above. Terrell's[7] report is fragmentary and incomplete and the process had begun well before the menopause. Kopp[10] frankly lays the blame on puberty as the only etiological factor. Gaucher and Crouzon[14] made a rather incomplete analysis of their case, a woman, aged twenty-eight years, upon whom an ovariotomy was performed after six years of pelvic inflammatory disease. The question of syphilis was apparently not considered. The relation of the ovariotomy to the telangiectases suggests the chronological rather than etiological. The cardiovascular changes of Basedow's disease were present in the 2 cases of hyperthyroidism (Létienne et Arnal[11] and Hyde[19]).

SITE OF ONSET OF THE TELANGIECTASES. Investigation of the site of onset was made in the hope of determining whether there was a possible *locus minoris resistentiæ* for this disease and what deductions might be drawn from it. It was found that 6 cases had begun upon the face, 8 below the elbows, and 10 below the knees. Only 7 appeared upon the remaining parts of the body. The localization to the most dependent portions of the body of 18 out of 33 cases at onset is decidedly of interest as indicating that the lesion tends to occur in the weakest part of the peripheral circulatory system. The involvement of the face in hyperthyroid cases was explained by Hyde[19] on the ground that it was a highly vascularized site, close to the heart, and subject to "special exposure to the bombardment of the left ventricle." This rather plausible explanation seems applicable to the entire range of cases under consideration. It justifies the inclusion of the face with the parts of least resistance in the peripheral vascular system.

ASSOCIATED DERMATOLOGICAL CONDITIONS. While a considerable variety of dermatoses appeared in individuals affected with general telangiectasia, the following were the only conditions whose constancy suggested a relation to the vascular abnormalities.

Urticaria	3 cases.
Dermatographia	4 "
Vasomotor asthenia, pronounced	3 "
Tertiary syphilides	4 "
Nevi (numerous)	2 "
Edema (Fearnsides' syndrome)	5 "

Allowing for one case counted twice, 9 cases in a total of 28 presented cutaneous conditions commonly associated with peripheral vascular changes. If edema be included the total rises to 14 out of 28 cases.

Lesions Present. With a view to ascertaining whether the clinical descriptions could be combined to form an approach to an average type, the separate lesions described were catalogued as follows. Practically every case presented several types at once and accordingly appears under a corresponding number of entries:

Macules	19 cases.
Papules	3 "
Puncta (angiomatous)	7 "
Diffuse undifferentiated erythema	9 "
Bands	3 "
Aborescences and visible telangiectatic network	18 "
Mottled areas (livedo or *cutis marmorata*)	4 "
Annular and gyrate figures	2 "
Induration in the lesions (excluding papules)	9 "
Secondary changes (in 26 cases):	
Atrophy	3 "
Pigmentation	5 "
Depigmentation	2 "
Scaling	11 "
Purpura	5 "

From this *resume* certain objective features seem to stand forth with some definiteness. The efflorescence is a combination of macules and arborescences, with a certain amount of diffuse erythema. About 25 per cent. of the cases show some slight induration on palpation. Annular and gyrate figures are an insignificant part of the picture, which differentiates it rather sharply, morphologically from the angioma serpiginosum group, as does also the relative unimportance of the "cayenne pepper grain." Atrophy and depigmentation, similarly, are uncommon secondary changes, while slight scaling ranks as the commonest. Even this is easily overemphasized, so that typically the telangiectasia exists without apparent secondary change in the affected skin. On objective grounds alone then, there seems to be good reason for differentiating the syndrome under discussion from that of angioma serpiginosum and Majocchi's disease.

Symptoms. Itching was present in moderate degree in 7 cases, absence of symptoms specially noted in 6 cases, no mention made of the subject in 19 cases.

Blood Examination. Examined in 7 cases, normal in 4 cases. One case had a red count of 6,500,000 (Trawinski)[21] and 3 per cent. of mast cells. Two cases showed moderate secondary anemia, the first of them with leukopenia. The second was Chauffard's[9] case of hemophilia, with lowered coagulation time and leukocytosis.

Mucous Membrane Lesions. In 8 cases in which the mucous membranes were specially examined, 3 were involved and 5 were not.

Prognosis. While under observation, 8 cases remained stationary and 6 progressed. Death occurred from the following causes in 4 cases: cerebral and general arteriosclerosis, hemiplegia, terminal pneumonia (Ehrman);[17] chronic ulcerative iliocolitis following typhoid, with marasmus, edema and acute endocarditis (Fearnsides);[22] generalized visceral tuberculosis with chronic diarrhea, marasmus, and edema (Fearnsides); suicide (Frick).[23] Autopsy on this case showed carcinoma of the liver, of much more recent origin than the telangiectasis.

Improvement was noted in 4 cases, 3 of which were suffering from diarrhea and edema (Fearnsides). Two cures are recorded, one by Fearnsides, which occurred when the child's diarrhea was gotten under control, and one by Ehrmann. The latter case was one of syphilis of two years' standing, in which a patch of telangiectasis the size of a palm appeared on the hip. It cleared up in the course of two years of mercurial treatment. Mercury, on the other hand, is stated to have had no effect in three other old syphilitics (Mandelbaum,[4] Lanceplaine III[15] and Trawinski[21]).

SUMMARY OF THE LITERATURE. The impressions gathered from the foregoing comparative review of the literature may be summarized as follows:

1. It would appear that from a number of reported examples of so-called primary, idiopathic, or essential cases of generalized telangiectasia it is possible to segregate a new group on the basis of certain clinical considerations. In this group, well-known factors in cardiovascular pathology, such as syphilis, chronic plumbism, hyperthyroidism, and nephritis, may be suspected of forming the etiological background for the cutaneous manifestations.

2. Clinical examination and autopsy by revealing extensive cardiovascular disease, further support the suspicions aroused by this association and lend color to the belief that the cutaneous manifestations are simply unusual phases of the general involvement.

3. In the list of cardiovascular degenerative agents here enumerated, first rank must be assigned to syphilis.

4. The absence of annular and serpiginous lesions in the majority of the cases, the insignificant part played by atrophy, hemorrhage, depigmentation, follicular involvement, etc., would seem to differentiate it clinically from Majocchi's disease and angioma serpiginosum. The picture is a relatively simple one from the stand-point of clinical description—macular lesions and arborescent telangiectases with a certain amount of diffuse erythema; occasionally angiomatous puncta; slight induration on palpation in perhaps one-fourth of the cases. The most notable secondary change is a moderate scaling.

5. To this clinical picture my case in the main conforms, both from the stand-point of presumptive etiology and objective characteristics.

DISCUSSION OF THE PATHOLOGY. Thus far the discussion of the possibility of regarding certain of the so-called "essential" forms of the generalized telangiectases of the skin as simply rare aspects of the vascular pathology of syphilis, lead-poisoning, etc., has been confined to clinical considerations. It is unfortunate that a parallel comparative study of the local pathology cannot be carried out, owing to the fact that of the 33 cases here considered only 7 were subjected to histopathological investigation. Of the 7 available reports, several are fragmentary. The available material may be briefly reviewed as follows:

Mandelbaum's[4] Case: Histopathological examination by Stroganoff. Patient was an old syphilitic with macular, arborescent, and even nodular telangiectatic and angiomatous lesions, generalized over most of the body. The pathological changes consisted of moderate atrophy of the papillary body, with marked hyperpigmentation. New formation of bloodvessels was apparent in the subpapillary rete. The ectasia was not accompanied by any thickening of the perithelial connective tissue or changes in the endothelium.

Gastou's[5] Case I: Histopathological examination by Darier. Old syphilitic with advanced central nervous manifestations. Daughter developed general telangiectases also. The father presented a generalized telangiectasia of a plexiform type with large patches and mottled areas suggestive of ecchymoses. Fragmentary report. Moderate perivascular infiltrate the only positive finding. No pronounced ectasia apparent.

Ehrmann's[17] Case IV: Picture of generalized arteriosclerosis and endarteritis. Lethal exit following hemiplegia at forty-five years. Telangiectases and livid mottled patches over trunk and extremities. Blueness and mottling of hands and feet. Suggestion of purpura about the feet. Histopathological examination of the skin showed endarteritis of the finer capillaries of the affected skin, comparable to that described for Raynaud's disease. From this finding Ehrmann argues that localized sclerosis of the skin vessels may give the clinical picture of telangiectasia. The mechanism operates in his opinion, through the accumulation of blood in the arteriovenous network as a result of the diminished elastic recoil of the arterioles. While not making the vascular changes synonymous with syphilis, he lays great stress upon its etiological importance, and in addition to the 4 cases reported, mentions that he has seen 3 other cases of peripheral cutaneous vascular disturbance associated with late lues. A second paper (1908),[18] to which the writer has unfortunately not been able to secure access, presumably further analyzes this point of view and extends its application.

T. C. Fox's[20] Case: Grouped papular telangiectases on the trunk, appearing in association with an obscure syndrome of vasomotor asthenia, rectal hemorrhages, and epistaxis in childhood. The histopathological study disclosed nothing more than vascular dilatation.

Trawinski's[21] Case: Macular, arborescent, and striate telangiectases in direct association with gummatous infiltrates in the skin. A careful histopathological study disclosed atrophy of the papillary body and vascular changes enumerated as follows: (1) dilatation; (2) marked perithelial proliferation with thickening of vessel walls; (3) some perivascular round-cell infiltrate; (4) involvement of the media in certain vessels, but apparent absence of pathological change in the endothelium; (5) no signs of hemorrhage. There was no follicular involvement. Numerous plasma cells were demonstrated with polychrome methylene-blue and occasional discrete collections of round cells. So striking was the pathological change in the vessels that Trawinski proposes the designation *perivasculitis syphilitica telangiectatica* for the picture as a whole.

Fearnsides'[22] Case I: Generalized tuberculosis with diarrhea and edema; lethal outcome. A rather indefinite report mentions dilatation and extravasation of blood around some of the smaller vessels and the absence of infiltration. The findings at least substantiate the view that the telangiectases and edema were due to actual injury to the vessel wall.

Frick's[23] Case: Generalized telangiectasia, indefinite syndrome. Autopsy showed carcinoma of the liver with metastases, more recent than the skin lesions. Rather indefinite biopsy findings seem to establish nothing except vascular dilatation.

It is apparent that no trustworthy general conclusions can be drawn from these findings. My case (see page 677) would seem to align itself with those of Ehrmann and Trawinski, both of which showed very definitely the minute changes of peripheral vascular sclerosis, and both, as in my case, in association with syphilis.

While in general angioma serpiginosum has been excluded from the foregoing consideration of generalized telangiectasia, the pathological study of Wise's[24] case, conducted by Pollitzer, is an exceptionally complete one, and the findings present several striking points of resemblance to those in the present case. For that reason they are here briefly reviewed. The epidermal changes in Wise's case consisted of marked intracellular edema with some round-cell infiltration of the deeper parts of the rete Malpighii and the basal layer. In certain of the indurated lesions this process was a striking feature of the picture. It will be recalled as present to only a slight degree in my case just described. Apart from some edema and degeneration of the collagen in Wise's case the principal changes in the corium were vascular, and include new formation of capillaries, many of them abnormally sinuous, endarteritis, and moderate perivascular lymphocytic infiltration (early stages). These cells often form single rows or collars about the adventitia of the smaller vessels. The condition did not apparently progress to the point of complete obliteration of the vessel lumina. Summarizing, Pollitzer repudiates the idea that the picture thus presented is that of an angioma, and characterizes it as "a low-grade inflammation, affecting primarily the capillary areas of the papillary and subpapillary rete, with secondary effects in the epidermis."

Reference to my description and figures will call attention to the really remarkable resemblances between Pollitzer's account of Wise's case and the author's own. That Pollitzer was fully alive to the questions raised by the dissimilarity between Wise's case and the conventional histopathological architecture of angioma serpiginosum is evidenced by the following statement: "It seems equally certain that there has been included in this group (angioma serpiginosum) another class of cases with similar clinical appearances which is of an entirely different nature anatomically and etiologically. One is a progressive superficial capillary hemangioma, the other a subacute inflammatory process, limited to the papillary and subpapillary layers, most probably of toxic origin."

In the light of the foregoing considerations it must be conceded that exclusively clinical studies have failed to properly differentiate the widespread acquired vascular dilatations affecting the skin. Resort must be had to complete and thorough investigation of the etiological possibilities in the individual case and to systematic biopsy and histopathological study.

I regret that inability to secure Majocchi's original paper[25] on purpura annularis telangiectodes and a lack of pathological material illustrative of this rare dermatosis make it inadvisable to institute searching comparisons between my case and the group just mentioned. According to a summary by Trawinski,[21] obliterative endarteritis with its sequelæ in atrophy and sclerosis of the cutis forms the basis of the pathological picture. Majocchi is quoted as advancing an angioneurotic hypothesis and a theory of direct action by some toxin upon the vessels themselves. According to the latter view, cardiac disease, lues, infectious diseases, etc., any toxin or toxin-producing agent which can excite endothelial reaction and proliferation may serve as the basis for Majocchi's syndrome. The acceptance of such a view would seem to include purpura annularis telangiectodes in an etiology shared by cases of the essential type. The occurrence of hemorrhage, so often emphasized as a differential point in Majocchi's disease as against the other telangiectatic syndromata, would seem to lose much of its force when it is recalled that weakening of a vessel wall in a sclerotic process not infrequently results in rupture. Such an occurrence is familiar enough in the brain in the various forms of cerebral hemorrhage due to arteriosclerosis. Furthermore, obliterative endarteritis in Majocchi's disease may bear the same relation to cutaneous atrophy and fibrosis that anemic infarct due to obliterative endarteritis of the terminal vessels of the coronary system bears to fibrosis and sclerosis in the heart muscle.

CONCLUSIONS. 1. Cardiovascular degenerative conditions, among which syphilis is most conspicuous, appear to stand in etiological relation to a considerable percentage of the obscure dermatoses heretofore grouped under the meaningless terms "essential," "idiopathic," and "primary" telangiectasia.

2. The conception of a low-grade inflammation due to definite etiological factors, such as syphilis, lead, alcohol, hyperthyroidism, etc., forms a more substantial starting-point for further study than relatively intangible angioneurotic theories of the etiology of generalized telangiectases.

3. Much of the existing confusion in the classification of telangiectatic cutaneous lesions can be ascribed to overreliance on purely clinical data, whose value as exclusive criteria in these cases is open to grave doubt.

4. While not all acquired cutaneous telangiectases will be aligned under the schema just mentioned, there is reason to believe that more searching analysis of etiology and pathology will readjust classification in this field. Such study may even lead to the inclusion of clinical cases of angioma serpiginosum or Majocchi's disease under a new group of peripheral vascular scleroses with telangiectasia of known etiology.

I feel it a privilege to acknowledge the cordial coöperation of my chief, Professor Wile, in the form of invaluable criticism and suggestions bearing on the work and in the generous use of departmental facilities. I also acknowledge with thanks the courtesy and interest of the members of the clinical faculty whose examinations have contributed so materially to the thoroughness of the investigation where it concerned the fields of their special departments.

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ON THE USE OF STRYCHNIN IN BROKEN CARDIAC COMPENSATION.[1]

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Many English and American clinicians are in the habit of prescribing strychnin for persons suffering from acute and chronic heart failure. Strychnin is used for this purpose because it is believed that it increases the work of the heart and that it slows and steadies the pulse. Yet an unbiased examination of the evidence will show that there is no sound basis for this belief. Pharmacologists have not been able to demonstrate that strychnin increases the output from the heart. Clinicians have not shown that broken cardiac compensation can be relieved by strychnin. But since physicians continue to employ strychnin in the treatment of heart disease despite these facts, it is important to furnish data about which there can be no reasonable doubt. Such data, to be absolutely convincing, must be quantitative. One may measure the effect of a drug on broken cardiac compensation by recording the rate of the pulse, the rate of the respiration, the weight, the fluid intake, and the urinary output, before, during, and after its administration.

Earlier Studies. *Pharmacological Observations.* Igersheimer,[2] in 1905, reviewed the work of earlier observers and added important new data. It is to be noted that the pharmacologists always used amounts of strychnin which were many times the therapeutic dose—amounts which invariably caused convulsions. For example,

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[2] Ueber die Wirkung des Strychnins auf das Kalt und Warmblüherherz, Arch. f. exp. Path. u. Pharm., 1905, liv, 73.